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Osthole Decreased Renal Ischemia-Reperfusion Injury by Suppressing JAK2/STAT3 Signaling Activation

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Objective: Renal ischemia-reperfusion (I/R) injury is a major cause of acute kidney injury. The pathogenetic mechanisms of renal I/R injury involve in inflammation, oxidative stress and apoptosis. Osthole, a natural coumarin derivative has potential anti-inflammatory effect. This study was to investigate the effect of osthole in renal I/R injury and its potential mechanism.
Methods: We induced renal I/R injury by clamping the left renal artery for 45 minutes followed by 24 hours of reperfusion with the contralateral nephrectomy. We randomly assigned 70 rats to 7 groups ($n = 10$): Sham, IRI, and osthole 0, 5, 10, 20, 40 mg/kg groups. We treated rats intraperitoneally with osthole for 45 minutes before renal ischemia. We harvested serum and renal tissue at 24 hours after reperfusion. Renal function and histological changes were assessed. Moreover, the expression of tumor necrosis factor-alpha (TNF-α), interleukin-8 (IL-8) and interleukin-6 (IL-6) in renal tissue and serum were examined by RT-PCR and ELISA, respectively. The expression of p-p65, p65, p-JAK2, JAK2, p-STAT3 and STAT3 were measured by Western blotting.
Results: Osthole pretreatment can significantly attenuate renal dysfunction in a dose-dependent manner, histological changes, the expression of TNF-α, IL-8, IL-6, p-JAK2, p-STAT3 and p-p65 induced by renal I/R injury. But neither osthole nor I/R injury have influence on the expression p65, JAK2 and STAT3.
Conclusion: Osthole pretreatment can decrease renal ischemia reperfusion injury by abrogating inflammation and the mechanism is partially involved in suppressing JAK2/STAT3 activation. Thus, osthole may be a novel practical strategy to prevent renal I/R injury.

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Septic Acute Kidney Injury in Critically Ill Patients: Incidence, Clinical Characteristics and Outcomes

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Objective: The etiology of acute kidney injury (AKI) in critical care setting is often multifactorial. However, sepsis has consistently been found to be a leading cause. The objective of this study is to examine the incidence, clinical characteristics and outcome (90-day mortality) of critically ill patients with septic AKI.
Methods: Patients admitted to the ICU of one regional hospital between 1/1/2011 to 31/12/2013 were included, excluding those who were already on chronic renal replacement therapy. AKI was defined using KDIGO criteria. Patients were followed till 90 days from ICU admission or death, whichever occurred earlier. Demographics, diagnosis, clinical characteristics, severity of kidney injury and outcome were analyzed.
Results: A total of 3687 patients were included, and 2018 (54.7%) patients developed AKI. Sepsis was the most common cause of AKI (49.2%) followed by hypovolemia (32.3%), cardiogenic (14.1%) and others (4.4%). Compared to those without AKI, AKI patients had higher disease severity, more physiological and biochemical disturbance, and carried significant co-morbidities. 90-day mortality increased with severity of AKI (16.7%, 27.5%, 48.3% for KDIGO stage 1, 2 and 3 AKI, $p < 0.001$). Full renal recovery was achieved in 71.6% of AKI patients. Compared with non-septic AKI, septic AKI was associated with higher disease severity and required more aggressive support. Non-recovery of renal function occurred in 2.5% of patients with septic AKI, compared with 6.4% in non-septic AKI ($p < 0.001$). Cox regression analysis showed that age, emergency ICU admission, postoperative cases, admission diagnosis, etiology of AKI, disease severity score, mechanical ventilation and vasopressor support, blood parameters (like albumin, potassium and pH) independently predicted 90-day mortality.
Conclusion: AKI, especially septic AKI is common in critically ill patients and is associated with poor patient outcome. Etiology of AKI has a significant impact on 90-day mortality and may affect renal outcome.

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Role of Long-term Label Retaining Cells in Regeneration Process of Ischemia-Reperfusion Injured Mouse Kidney

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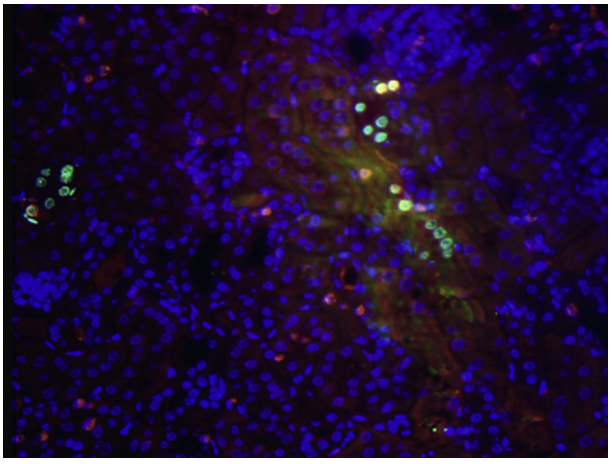
Objective: The study intrinsic renal stem cells in kidney injury repair process in the role, clear intrinsic renal stem cells involved in wound healing. Explore new methods for the treatment of kidney disease. Discusses the kidney inherent stem cell in kidney distributed spot, for further separates the purification and the function research lays the foundation.
Methods: (1) Renal ischemia/reperfusion (I/R) injury model: mice were anesthetized with chloral hydrate. The renal artery and vein were isolated from surrounding tissues and kidneys were subjected to ischemia by clamping bilateral renal pedicles with non-traumatic mirovascular clamps for 22 minutes. (2) Assessment of renal function: serum creatinine (Scr) and blood urea nitrogen (BUN) were monitored. (3) Collect the complete experimental animal blood serum and the organization specimen. Use serology examination, histochemistry examination and correlation Western blot and RT-PCR examination. (4) Quantification of BrdU-positive cells: determined by counting the number of positive nuclei on 5 selected fields of sections in a blinded manner by a light microscope at 200×. The average number of the 5 fields was recorded as the number of BrdU-retaining nuclei per field.
Results: (1) Long-term renal LRCs exhibited multiple biological characteristics during the recovery process after I/R injury in mouse kidneys. (2) Adult kidneys had spontaneous capability to restore from acute injured renal function, future studies will be required to clarify which types of renal cells repair injured kidney and the remodeling mechanism of acute injured kidneys, so as to develop targeted treatments for AKI.
Conclusion: (1) The restoration of renal function and structure in mice after I/R injury. (2) The distribution of long-term LRCs in mouse kidney after I/R injury. (3) Not all of long-term LRCs play a positive role in the regeneration process of I/R injured kidneys. (4) The phenotype of long-term LRCs in mouse kidneys after I/R injury.



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